

APPENDIX II
CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(3)

42. A method of constructing a population of altered heavy chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference nucleic acid sequence comprising the sequence of a donor heavy chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor heavy chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, each encoding at least one modified complementarity-determining region, wherein said modified complementarity-determining region comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence; and ii) a second population of oligonucleotides, comprising oligonucleotides encoding modified portions of a heavy chain variable region framework, said modified portion containing a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence;

c) mixing said first and second populations of oligonucleotides under conditions such that at least a portion of said oligonucleotides hybridize so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered heavy chain variable region encoding nucleic acids is constructed.

43. The method of Claim 42, wherein said representation of first and second reference sequences is in electronic form.

44. The method of Claim 42, further comprising the step of (e) coexpressing said population of altered heavy chain variable region encoding nucleic acids with a light chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

45. The method of Claim 42, wherein said synthesizing comprises chemically synthesizing.

46. The method of Claim 42, wherein said acceptor is human.

47. A method of constructing a population of altered light chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference nucleic acid sequence comprising the sequence of a donor light chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor light chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, each encoding at least one modified complementarity-determining region, wherein said modified complementarity-determining region comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence; and ii) a second population of oligonucleotides, comprising oligonucleotides encoding modified portions of a light chain variable region framework, said modified portion containing a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence;

c) mixing said first and second populations of oligonucleotides under conditions such that at least a portion of said oligonucleotides hybridize so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered light chain variable region encoding nucleic acids is constructed.

48. The method of Claim 47, wherein said representation of first and second reference sequences is in electronic form.

49. The method of Claim 47, further comprising the step of (e) coexpressing said population of altered light chain variable region encoding nucleic acids with a heavy chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

50. The method of Claim 47, wherein said synthesizing comprises chemically synthesizing.

51. The method of Claim 47, wherein said acceptor is human.